Heterocyclic analogs of o-xylylene

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CHAPTER V

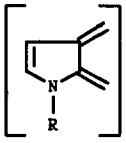
Investigations of 4-substituted 2,3-dimethylene-2,3-dihydropyrroles. Synthesis and reactions of Me_3SiCH_2-TosMIC

Investigations of the synthesis of precursors **5.4** of 4-substituted 2,3-dimethylene-2,3-dihydropyrroles (**5.2**) are described in this Chapter. The route that was selected for the synthesis of the precursors **5.4** is discussed in the Introduction 5.1. The results obtained for the synthesis of the precursors **5.4** are described in Section 5.2.1. Reactions of Me_3SiCH_2-TosMIC are presented in Sections 5.2.2 and 5.2.3. In Section 5.2.4, reactions of *N*-methyl-3,4-disubstituted-2-(trimethylsilylmethyl)-pyrroles are presented. The synthesis and reactivity of 2,3-dimethylene-2,3-dihydrothiophene (**3.1a**) were described in Chapters II and III, respectively. Attempted formations of the 3,4-substituted thiophene isomer of **3.1a** (i.e. **4.2**) were described in Chapter IV.

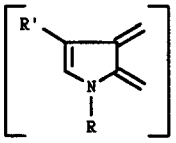
5.1. INTRODUCTION

2,3-Dimethylene-2,3-dihydropyrrole (**5.1a**) and the *N*-protected diene **5.1b** (Chart 5.1) are two of the possible pyrrole analogs of *o*-xylylene (**3.7**).* So far no such pyrrole analogs of *o*-xylylene have been reported. In Section 1.2, a survey is given of the known heterocyclic analogs of *o*-xylylene. Some 2,3-dimethylene-2,3-dihydroindole derivatives have been reported; these are closely related to the unknown pyrrole species of type **5.1**. We decided to generate **5.1** and **5.2** from the precursors **5.4** by a fluoride-induced elimination of Me_3SiF and R_3N.[1] Our preference for Saegusa's method[1] to generate such dienes has been discussed in Chapter I.

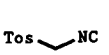
Chart 5.1.



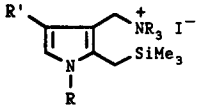
5.1



5.2



5.3



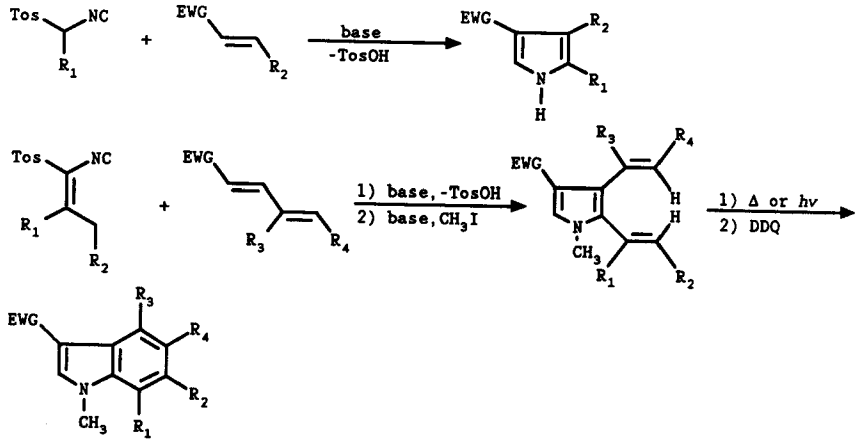
5.4

* The first digit of the compound number represents the Chapter in which the compound is described first, or in which it is discussed in detail.

The synthesis of the precursors **5.4** is fairly complex. Pyrroles are more reactive towards electrophiles and less stable than thiophenes.[2] Although it should be possible to synthesize the precursors **5.4** with the use of the methodology described in Chapter II, for instance, precursor **2.5** of 2,3-dimethylene-2,3-dihydrofuran has been synthesized in that way by Gregor and Wiseman[3] (see Chapter II, Scheme 2.4), we decided to follow a completely different strategy.

Our research group has considerable experience in the synthesis of (substituted) pyrroles[4] and other (substituted) heterocycles like oxazolines, oxazoles[5] and indoles[4d] (Scheme 5.1). For the synthesis of such heterocycles tosylmethyl isocyanide (TosMIC) and derivatives are quite useful. TosMIC[6,7] (**5.3**), discovered[6a] in 1967, reacts with Michael acceptors to provide pyrroles, with ketones to give oxazolines and with aldehydes, oxazoles and oxazolines are obtained. These reactions have been rationalized as base-induced additions of TosMIC to the electrophilic substrates, followed by ring closure to the isocyanide carbon and subsequently, if an appropiate hydrogen is present, elimination of *p*-toluenesulfinic acid.[7]

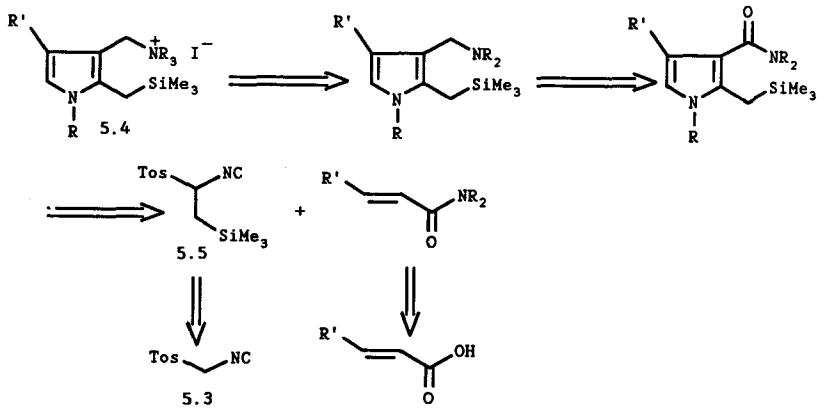
Scheme 5.1.



2,3,4-Trisubstituted pyrroles, bearing electron-withdrawing substituents at C-4, have been synthesized with substituted TosMIC derivatives, as is shown in Scheme 5.1. An electron-withdrawing group (EWG) must be present, since the pyrrole

synthesis begins with a Michael addition. Thus, the "TosMIC-strategy" limits us to study substituted pyrrole dienes of type **5.2**, which bear an electron-withdrawing group at C-4.

Scheme 5.2.



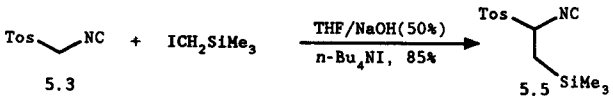
A retrosynthetic analysis of the synthesis of precursor **5.4** based on the chemistry of TosMIC is outlined in Scheme 5.2. For the synthesis of precursor **5.4** α-(trimethylsilylmethyl)tosylmethyl isocyanide (Me_3SiCH_2-TosMIC) and a Michael acceptor bearing a potential ammoniumalkyl group and an effective EWG were needed. As the potential ammoniumalkyl group we have selected the tertiary amide group for two reasons. Firstly, the amide function is a weak director in Michael addition reactions,[8] which is important to obtain the correct regio specificity in the addition reaction of the anion of Me_3SiCH_2-TosMIC. Many groups, such as PhCO, SO_3Ph, CHO, MeCO, CO_2Ph, *p*-$TolSO_2$, CO_2Me and CN are stronger directors.[17] We have used PhCO and CO_2R for R', because of the easy availability of the Michael acceptors. Secondly, deuterium can be incorporated by reduction of the amide function with $LiAlD_4$. The deuterium analog can be used to determine the regioselectivity of the dimerization of the pyrrole diene, analogously to the thiophene diene **3.1a** (as described in Chapter III).

5.2. RESULTS AND DISCUSSION

5.2.1. The synthesis of Me_3SiCH_2-TosMIC (5.5)

TosMIC has been alkylated to provide mono- and disubstituted derivatives. Selective monoalkylation has been achieved earlier under phase transfer conditions.[9]

Scheme 5.3.



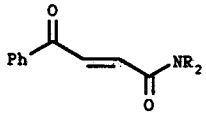
5.3 5.5

Reaction of TosMIC with Me_3SiCH_2I[10] (a modified synthetic procedure of which is described in Chapter II) gave the mono-alkylated product **5.5** in 85% yield, using *n*-Bu_4NI as a PTC catalyst in THF/ 50% aqueous NaOH (Scheme 5.3). A slight excess (1.2 equivalent) of Me_3SiCH_2I was necessary to achieve complete reaction. The reaction was faster when THF was used as organic solvent instead of CH_2Cl_2, which is more commonly used in phase transfer reactions.[11] With CH_2Cl_2, the reaction was complete in ca. 4 h when 4 equiv of Me_3SiCH_2I were used. With THF and 2 equivalents of ICH_2SiMe_3 , the reaction was complete in 30 min. Recently, Magnus *et al.*[9c] have independently reported the synthesis of **5.5** in a yield of 51% from TosMIC and ICH_2SiMe_3 (1.8 equivalents) in CH_2Cl_2/30% aqueous NaOH using benzyltriethylammonium chloride as PTC catalyst.

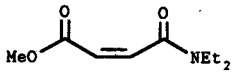
5.2.2. The synthesis of the Michael acceptors 5.6 and 5.7

In addition to the synthesis of isocyanide **5.5**, the Michael acceptors **5.6a**, **5.6b** and **5.7** (Chart 5.2) needed to be prepared as the substrates for the synthesis of the precursors **5.4.** The selection of the substituents of the Michael acceptors has been explained in Section 5.1.

Chart 5.2.



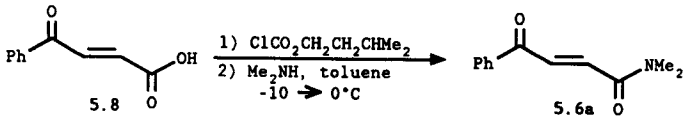
5.6a: R = Me
5.6b: R = Et



5.7

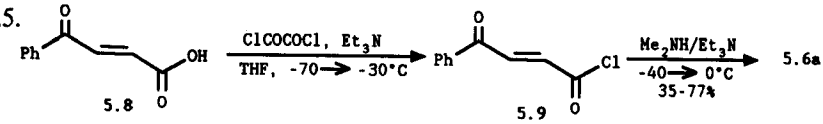
Benzoyl acrylamide **5.6a** has been described previously in a Japanese patent,[12] The compound was prepared as shown in Scheme 5.4.

Scheme 5.4.



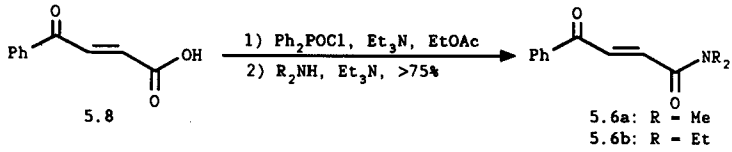
We have synthesized the unsaturated carboxamides **5.6** by two different methods. Firstly, we synthesized amide **5.6a** via acid chloride **5.9**[13] (Scheme 5.5) Acid chloride **5.9** was prepared *in situ* from carboxylic acid **5.8** and oxalyl chloride in the presence of triethylamine and, next, was treated with aqueous Me_2NH to give carboxamide **5.6a** (Scheme 5.5). The yields of **5.6a** varied considerable in this synthesis (34% - 77%). Several changes in the reaction conditions (temperature, amount of dimethylamine, reaction time) were investigated, but no improvement in reproducibility was obtained.

Scheme 5.5.



Attempts to synthesize pure diethyl carboxamide **5.6b**, analogously to **5.6a**, from **5.8** were unsuccessful. Amides **5.6b** and **5.6a** needed to be purified by bulb-to-bulb distillation. However, amide **5.6b** could not be purified effectively, owing to considerable losses by thermal decomposition.

Scheme 5.6.

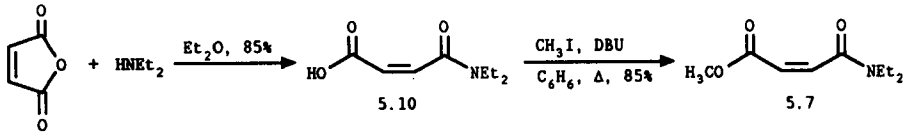


A better synthesis of the amides **5.6a** and **5.6b** from **5.8** is outlined in Scheme 5.6. Reaction via a mixed anhydride, prepared *in situ* from **5.8** and diphenylphosphoryl chloride,[14] gave a cleaner reaction product **5.6a** than via acid chloride **5.9** (Scheme 5.5). The crude reaction product was purified by chromatography and now

the yield was reproducible (82%). Acrylamide **5.6b** was synthesized via the mixed anhydride route in a yield of 75%.

Michael acceptor **5.7** has been described earlier.[15] Reaction of maleic anhydride with diethylamine gave acid derivative **5.10**. The esterification of **5.10** to **5.7** was accomplished by an alternative procedure, using DBU and methyl iodide in benzene[16] (Scheme 5.7).

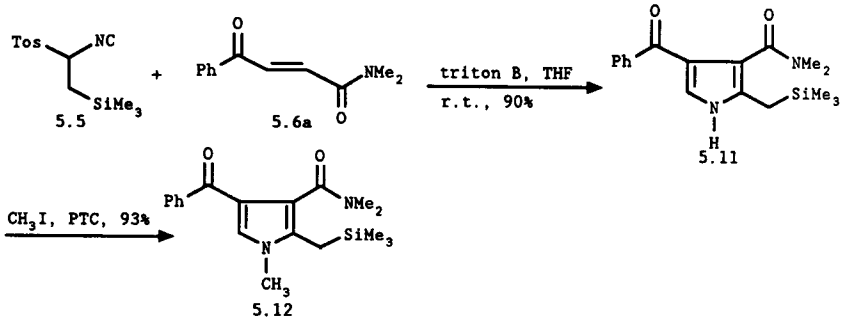
Scheme 5.7.



5.2.3. On the synthesis of the precursors 5.4a and 5.4b

Reaction of Me_3SiCH_2-TosMIC with benzoyl acrylamide **5.6a** gave the best results when Triton B was used as base. The reaction proceeded within 5 min at room temperature and pyrrole **5.11** was isolated in a yield of 90% (Scheme 5.8). When *t*-BuOK was used as base, complex reaction mixtures were formed, even at -70°C.

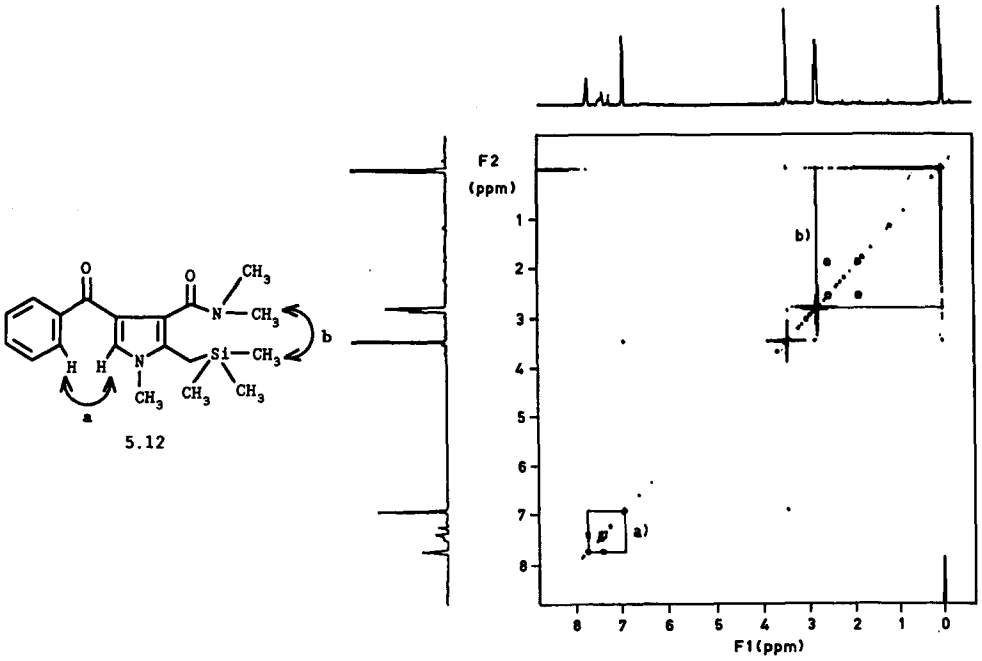
Scheme 5.8.



The regioselectivity of the reaction that gave pyrrole **5.11** was determined by NOESY (Nuclear Overhauser Enhancement Spectroscopy)[17] analysis of *N*-methyl pyrrole **5.12**, which was obtained from **5.11** in a yield of 93% (Scheme 5.8).

The NOESY spectrum of **5.12** is shown in Figure 5.1. The cross peaks between the α-protons of the benzoyl group and the pyrrole proton at C-5 [(a) in Figure 5.1] and between the protons of the Me_3Si-group and the protons of the dimethyl amide group [(b) in Figure 5.1] establish that **5.12** (and thus **5.11**) has the regiochemistry as depicted. Indeed, the benzoyl group is a stronger director than the carboxamide group in the Michael addition of **5.5** to **5.6a** (as was mentioned in Section 5.1).[17]

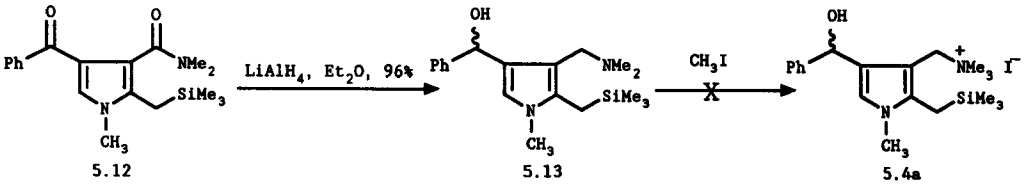
Figure 5.1: The NOESY spectrum[a] of *N*-methylpyrrole **5.12**.



[a]The spectrum was recorded in $CDCl_3$ by W. Kruizinga on a 300 MHz Varian VTR-300 apparatus.

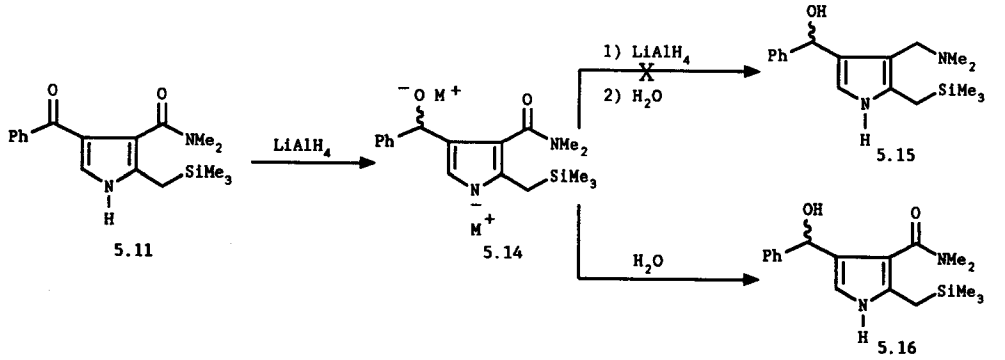
Both the carboxamide function and the benzoyl function of *N*-methyl pyrrole **5.12** were reduced with $LiALH_4$ (in an excess of 7.5 mole) to give hydroxymethyl-pyrrole **5.13** in 96% yield (Scheme 5.9).

Scheme 5.9.



In contrast, treatment of *N*-H pyrrole **5.11** with $LiAlH_4$ (in an excess of 3 - 5 mole) gave reduction of the benzoyl group only. We have observed (by ^1H NMR and IR) no reduction of the amide function of **5.11** to amine **5.15.** Hydroxypyrrole amide **5.16** was isolated in 75% yield from the reaction of **5.11** with $LiAlH_4$ (Scheme 5.10). The failure to reduce the carboxamide function of **5.11** to an amine group in this case is a result of deactivation of that carboxamide of **5.14** by the negatively charged pyrrole ring formed by deprotonation of the *N*-H (Scheme 5.10). Apparently, the ketone function of the negatively charged pyrrole ring is still reactive enough towards reduction. Generally, a ketone funtion is reduced more easily than an amide function.[18]

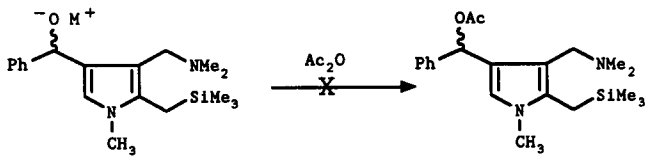
Scheme 5.10.



Quaternarization of the amine function of pyrrole **5.13** (Scheme 5.9) to precursor **5.4a** with methyl iodide was not successful. Under several conditions (refluxing acetonitrile, Et_2O at room temperature) immediately dark red colored reaction mixtures were obtained, in which no ammonium salt **5.4a** was detected (by ^1H NMR). Ammonium salt **5.4a** seemed to be unstable, probably owing to polymeriza-

tion. Polymerization may result by intermolecular nucleophilic attack of the hydroxy group at the trimethylammoniummethyl group of a second molecule of **5.13** or **5.4a**. *N*-Methylpyrroles, which bear a trimethylammoniummethyl group at C-3, have been described as stable solids.[19] Attempts to protect the hydroxy group of amine **5.13** by *in situ* acylation[20,21] (with Ac_2O) of reduction product **5.17** to acetate **5.18** (Scheme 5.11) were not successful. Dark colored reaction mixtures were formed, which did not contain the acylated product **5.18** (by ^1H NMR).

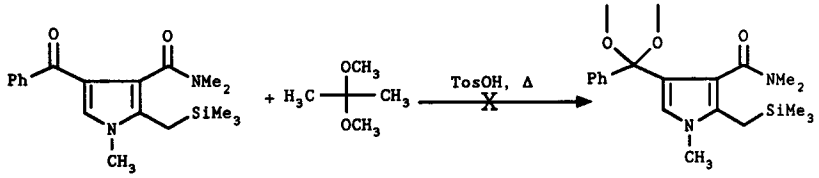
Scheme 5.11.



5.17 5.18

To avoid the formation of the hydroxy function (which probably causes the instability of ammonium salt **5.4a**) in the planned reduction of the amide function to a aminomethylpyrrole, we tried to protect the benzoyl function of pyrrole **5.12** by trans ketalization of the carbonyl group with 2,2-dimethoxypropane and a catalytic amount of *p*-toluenesulfonic acid. However, a dark colored reaction mixture was isolated, in which no product **5.19** was detected by ^1H NMR of the crude reaction product (Scheme 5.12). The crude reaction product was not purified further. The instability of pyrroles under acidic conditions may have caused this failure. Another explanation for the failure to obtain product **5.19** could be the vinylogous amide character of the benzoyl function of pyrrole **5.12**, which makes the carbonyl function of the benzoyl group less reactive compared to the carbonyl function of an ordinary ketone function.

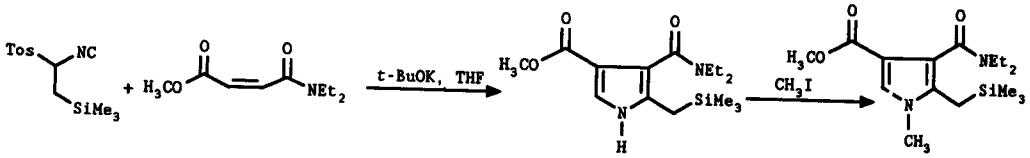
Scheme 5.12.



5.12 5.19

Reactions of isocyanide **5.5** with *N,N*-diethylcarbamoylacrylate **5.7** were not investigated thouroughly. We were not able to isolate pure pyrrole **5.20a** or methyl-pyrrole **5.20b** (Scheme 5.13). However, the *N*-H pyrrole, made from methyl-Tos-MIC and Michael acceptor **5.7** has been obtained pure (in moderate yield) by Leusink in our research group. It may perhaps be possible to obtain pyrroles **20a** or **20b** pure when Leusink's reaction conditions are used.[22]

Scheme 5.13.



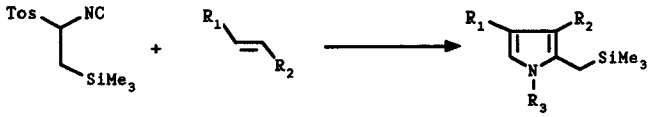
5.5 5.7 5.20a 5.20b

5.2.4. Reactions of Me_3SiCH_2-TosMIC 5.5 with some other Michael acceptors than 5.6 and 5.7

In addition to the synthesis of precursor **5.4a**, we have also investigated reactions of the anion of the new silyl derivative of TosMIC, Me_3SiCH_2-TosMIC (**5.5**) with Michael acceptors and alkyl halides, described in this Section and 5.2.5, respectively. The Me_3SiCH_2 group of **5.5** can be useful for further syntheses carried out with reaction products of **5.5**. For instance, we have used the Me_3Si group of pyrroles **5.23b** and **5.25b**, synthesized from **5.5** (Table 5.1, entries 3 and 5), for the formation of anions at the 2-methyl of **5.23b** and **5.25b**, which react with aldehydes and with a Michael acceptor (see below). This has been achieved by fluoride-induced desilylation of **5.23a** or **5.25b**. The results are described in Section 5.2.6.

The results of base-induced reactions of **5.5** with some Michael acceptors are outlined in Table 5.1. Isocyanide **5.5** reacts smoothly with Michael acceptors to give pyrroles **5.21a** to **5.25b** in good yields. Some pyrroles have been methylated to *N*-methylpyrroles (Table 5.1, entries 3,4 and 5), with or without isolating the *N*-H pyrrole. The pyrrole formed in reaction of **5.5** and (E),(E)-1,5-diphenylpenta-1,3-dien-5-one (Table 5.1, entry 5) is not stable (neither in solution nor in solid state) and was therefor methylated directly to **5.25b**, which is a stable solid.

Table 5.1. Pyrroles Synthesized from Me_3SiCH_2-TosMIC (**5.5**) and Some Michael Acceptors



5.5 5.21a-5.25b

Entry	Cond[a]	Compd	R^1	R^2	R^3	Yield (%)[b]
1	A	**5.21a**	PhCO-	-Ph	H	79
2	A	**5.22a**	MeO_2C-	-CO_2Me	H	74
3	B	**5.23b**	PhCO-	-CO_2Me	CH_3[c,d]	82
4	B	**5.24b**	PhCO-	-$CONEt_2$	CH_3[c,e]	77
5	A	**5.25b**	PhCO-	-C=C-Ph (*t*)	CH_3[f,g]	84

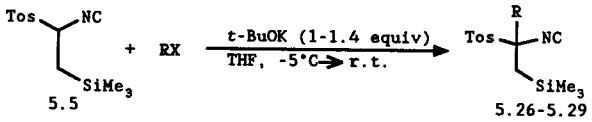
[a]Conditions: A: Me_3SiCH_2-TosMIC (1.0 equiv), Michael acceptor (1.0 - 1.5 equiv) and *t*-BuOK (2.2 equiv) in THF between -5 and 25°C: B: Same as A, using Triton B instead of *t*-BuOK. [b]Yields of isolated material after purification. [c]Methylation was carried out with *t*-BuOK/MeI in THF. [d]*N*-H Pyrrole was not isolated. [e]*N*-H Pyrrole was isolated in a yield of 94%. [f]Methylation was carried out under PTC conditions, using MeI, *n*-Bu_4NI in THF/aqueous NaOH (50%). [g]*N*-H Pyrrole is not stable.

The reaction of **5.5** with dimethyl fumarate (Table 5.1, entry 2) has been studied in some more detail. The reaction temperature needed to be between -5 and 25°C. At lower temperatures (-50°C) the reaction was too slow to achieve complete conversion in reasonable time. At higher temperatures a base-induced polymerization of dimethyl fumarate became a serious side reaction; even at room temperature an excess (1.5 equivalents) of dimethyl fumarate was necessary to achieve complete conversion of isocyanide **5.5**.

5.2.5. Base-induced alkylation reactions of Me_3SiCH_2-TosMIC (5.5)

Reactions of the anion of Me_3SiCH_2-TosMIC (**5.5**) with several alkyl halides were studied also. Isocyanide **5.5** reacted with alkyl halides to provide the di-substituted isocyanides listed in Table 5.2.

Table 5.2. Base-induced Alkylation Reactions With Me_3SiCH_2-TosMIC (**5.5**)



Entry	RX[a]	Compd	Yield (%)[b]	Mp (°C)[c]
1	MeI	**5.26**	92	88 - 90
2	EtI	**5.27**	81	80 - 81.5
3	$PhCH_2Br$[d]	**5.28**	70	125 - 126
4	H_2C=C-CH_2Br	**5.29**	79	[e]

[a]An excess of alkyl halide (6 - 16 equiv) was used, unless stated otherwise. [b]Yields of isolated material after purification. [c]Melting points of analytically pure product. [d]One equivalent of benzyl bromide was used. [e]Product **5.29** is an unstable oil at room temperature.

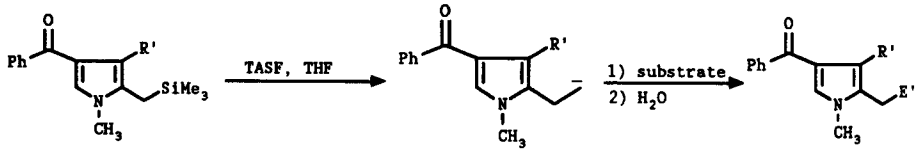
The alkylation of isocyanide **5.5** with non-bulky primary alkyl halides proceeded in good yields. Except in the case of benzyl bromide (Table 5.2, entry 3) an excess of alkyl halides was used. The excess of alkyl halide was necessary to achieve a good conversion of **5.5** to dialkylated products. The anion of **5.5** decomposes under the conditions of the reaction, but a fast reaction with the alkyl halide helps to improve the yield of alkylated products. The dialkylated products **5.26** to **5.28** are stable solids (Table 5.2, entry 5). Product **5.29** has been crystallized at -25°C, but it melted and decomposed when warmed to room temperature. Base-induced reactions of **5.5** with more bulky alkyl halides were not successful. When ICH_2SiMe_3 (1 equivalent) or isopropyl iodide (3 equivalent) were used, only impure starting

material **5.5** was recovered. No dialkylated products were present in the crude reaction product according to ^{1}H NMR.

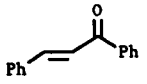
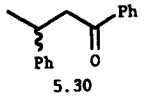
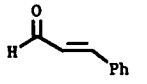
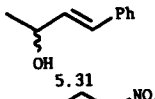
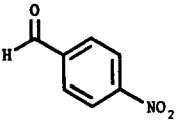
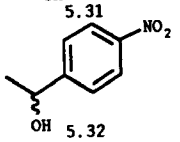
5.2.6. Reactions of some 3,4-disubstituted-1-methyl-2-(trimethylsilylmethyl)pyrroles

Treatment of *N*-methylpyrroles **5.23b** and **5.25b** with fluoride in the presence of an aldehyde or a Michael acceptor, gave the new C-2 substituted pyrroles **5.30** to **5.32**. The reactions are outlined in Table 5.3.

Table 5.3. Fluoride-induced Generation of α-Methyl Anions from 2-(Me_3SiCH_2)-methylpyrroles and Reactions thereof with Electrophiles.



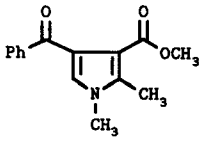
5.30-5.32

Entry	R'	Substrate	E'	Temperature (°C)	Yield[a](%)
1	-CO_2Me **5.23b**		 5.30	-50 to r.t.	40[b]
2	-C=C-Ph (*t*) **5.25b**		 5.31	r.t.	74[c]
3	-C=C-Ph (*t*) **5.25b**		 5.32	-70 to -20	66[d]

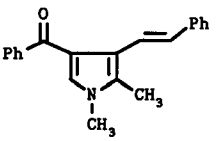
[a]Yields of purified material; the reactions have not been optimized. [b]Pyrrole **5.33** (Chart 5.3) and chalcone were also identified. [c]Pyrrole **5.34** (Chart 5.3) and cinnamaldehyde were also identified. [d]Product **3.32** partly decomposed during crystallization.

To the best of our knowledge this is the first demonstration of anions of (substituted) 1,2-dimethylpyrroles formed at the 2-methyl group. The reactions shown in Table 5.3 are not optimized. In entries 1 and 2 some chalcone or cinnamaldehyde and protodesilylated pyrrole **5.33** and **5.34** (Chart 5.3) were found in addition to the products **5.30** and **5.31**, respectively.

Chart 5.3.



5.33

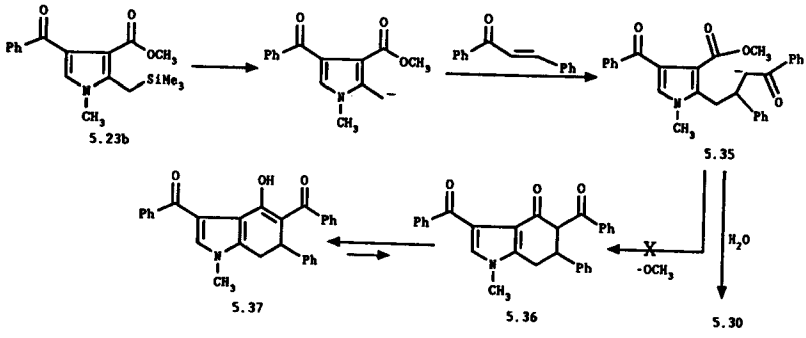


5.34

The formation of the hydroxy pyrroles **5.31** and **5.32** instead of the dehydration products of **5.31** and **5.32** [*i.e.* **5.38** and **5.41** (Scheme 5.15)] is not surprising. Desilylation of (substituted) benzylsilyl compounds in the presence of aldehydes gave previously 1-hydroxy-2-phenylethanes instead of styrenes.[23] The nitro function in *p*-nitrobenzaldehyde remained unaffected during the reaction. This is not to be expected when classical carbanion chemistry is used, which often causes electron transfer reactions involving the nitro function.[23a]

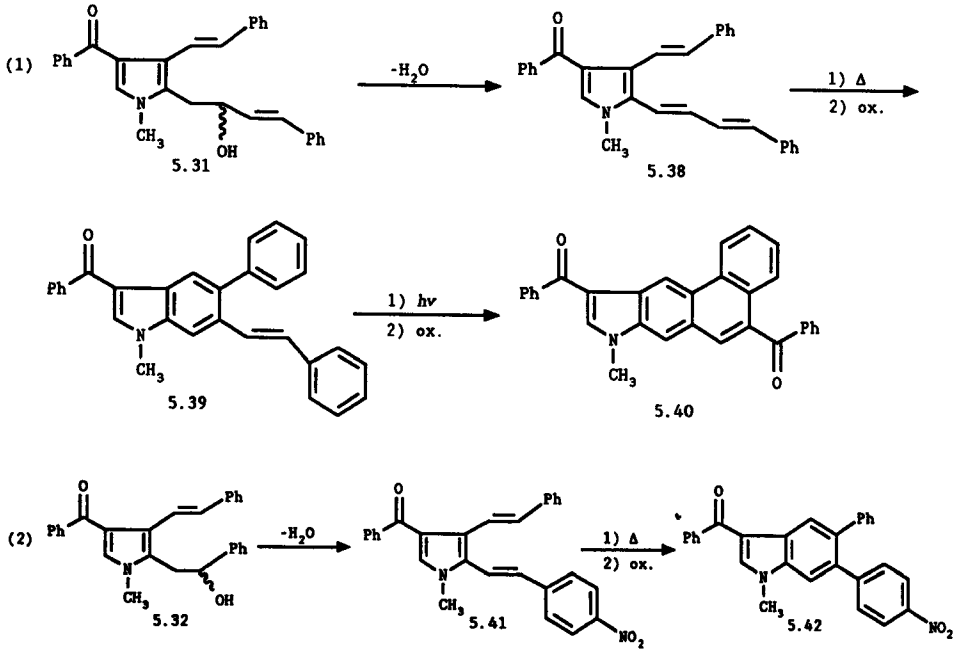
Unexpectedly, in the fluoride-induced reaction of pyrrole **5.23b** with chalcone no subsequent ring closure took place after the Michael addition (Scheme 5.14), although an electrophilic substituent is present at C-3. Analogously to the annulation reactions discussed in Chapters 1,3 and 4 of this thesis,[24] one would expect intramolecular nucleophilic attack of the Michael adduct anion **5.35** at the carbomethoxy group, which should give tetrahydroindole **5.36** or its tautomer **5.37**. The Michael adduct anion **5.35** appeared not reactive enough to undergo ring closure.

Scheme 5.14.



Pyrroles **5.31** and **5.32** are in principle precursors for indoles. For instance, dehydration of **5.31** should give pyrrole **5.38**, which contains a newly formed 6π-electron system. A sequential thermal or photochemical induced ring closure reaction and dehydrogenation step should give indole **5.39** (Scheme 5.15).[4d] Indole **5.39** could be subjected to a second ring closure and a dehydrogenation step, which should give naphtho[3,4-f]indole **5.40** (Scheme 5.15). Potentially, pyrrole **5.32** may be converted to indole **5.42** in a similar way (Scheme 5.15).

Scheme 5.15.



Unfortunately, dehydrations of **5.31** and **5.32** have so far not been successful. Attempts to dehydrate and cyclize pyrrole **5.31** in a one-pot procedure were not successful. Treatment of the pyrrole **5.31** in refluxing triglyme with an excess (10 equiv) of sodium acetate and acetic anhydride, which should *in situ* give the acetate of **5.31**, only provided recovered starting material **5.31**. The same negative result was obtained with pyrrole **5.32**. Treatment of pyrrole **5.32** in refluxing benzene with a catalytic amount of *p*-toluenesulfonic acid only gave recovered **5.32**. When a

catalytic amount of *p*-toluenesulfonic acid was added to pyrrole **5.32** in refluxing benzene, complex reaction mixtures were obtained. When the dehydration problems are solved, and it is likely that they can be solved, Me_3SiCH_2 substituted pyrroles should be useful precursors for the synthesis of indoles and annulated indoles.

5.3. EXPERIMENTAL SECTION

General: see section 2.3.
Samples of TASF (Fluka) were weighted in a nitrogen atmosphere.
The NOESY spectrum of pyrrole **5.12** (Figure 5.1), was recorded by W. Kruizinga on a 300 MHz Varian VTR-300 apparatus.

1-Isocyano-1-tosyl-2-(trimethylsilyl)ethane (Me_3SiCH_2-TosMIC, 5.5).[9c] A mixture of TosMIC (Ofichem) (59.5 g, 305 mmol), iodomethyltrimethylsilane[10] (Section 2.3, 78.4 g, 366 mmol) and *n*-Bu_4NI (11.1 g, 30 mmol, 10 mol-%) in THF (450 mL) was cooled in an icebath for 10 min. After the addition of aqueous NaOH (50%, 300 mL), the reaction mixture was stirred for 1.5 h at room temperature. Work-up by addition of Et_2O (500 mL) and water (500 mL), extraction with Et_2O (1 x 250 mL), washing of the combined ether layers with water (3 x 150 mL), drying (brine, $MgSO_4$) and removal of the solvents gave crude **5.5** (82 g). The crude material was extracted with hot petroleum ether (bp 80-110°C, 2 x 300 mL and 1 x 100 mL). The hot solution was decanted from insoluble polymeric material. Compound **5.5**, crystallized from the combined petroleum ether extracts, was collected and washed with pentane. Yield: 69.5 g, mp 107.5-108.5°C. Crystallization of the mother liquid (petroleum ether, bp 80-110°C) gave another portion of **5.5**. Yield 3.76 g, mp 105-108°C. Total yield: 73.3 g, 85%. Analytically pure material was obtained by recrystallization from hexane, mp 107-108°C (lit.[9c] mp 109-110°C). ^{1}H NMR ($CDCl_3$) δ 0.10 (s, 9H), 0.90-1.60 (m, 2H), 2.40 (s, 3H), 4.45 (dd, J = 12.0 and 3.6 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.82 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ -1.8 (q), 15.0 (t), 21.3 (q), 70.5 (d), 129.5 (d), 129.7 (d), 130.3 (s), 145.8 (s), 164.5 (s); IR (KBr) 3050, 2930, 2140, 1590, 1450, 1410, 1320, 1255, 1210,

1160, 1135, 1090, 1060, 1015, 930, 840, 745, 710 cm^{-1}.

Anal. Calcd for $C_{13}H_{20}NOSSi$: C, 55.28; H, 7.14; N,4.96; S, 11.35. Found: C, 55.39; H, 6.87; N, 5.06; S, 11.28.

(*E*)-*N,N*-Dimethyl-3-(benzoyl)acrylamide (5.6a). (a) Using diphenylphosphoryl chloride (DPPCl), triethylamine.[14] To a solution of 3-benzoylacrylic acid[25] (**5.8**, 880 mg, 5.0 mmol) in ethyl acetate (50 mL) was added at -80°C sequentially DPPCl (0.96 mL, 5.0 mmol) and triethylamine (0.72 mL, 5.0 mmol). The reaction mixture was stirred for 30 min, allowing the temperature to rise to -40°C. A solution of aqueous Me_2NH (40%, 0.70 mL, ca. 5.5 mmol) and triethylamine (0.72 mL, 5.0 mmol) in ethyl acetate (10 mL) was added all at once. The temperature rose to -20°C. The reaction mixture was stirred for 30 min at -10°C. Work-up by addition of water (50 mL) and Et_2O (50 mL), washing of the ether layer with NaOH (25 mL of a 7% aqueous solution) and a saturated NH_4Cl solution (10 mL), drying ($MgSO_4$) and removal of the solvents gave an oil (1.27 g), which was purified by flash chromatography (silica gel, Et_2O). Yield: 834 mg (82%) of **5.6a** as an yellow solid, mp 69.5-70.5. Analytically pure material was obtained by crystallization from ethyl acetate/hexane, mp 70.5-71.5°C: ^1H NMR ($CDCl_3$) δ 3.05 (s, 3H), 3.18 (s, 3H), 7.40-7.70 (m, 4H), 7.85-8.20 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 35.2 (q), 36.9 (q), 128.1 (d), 128.2 (d), 132.0 (d), 133.0 (d), 133.1 (d), 138.3 (s), 164.4 (s), 188.9 (s); MS *m/z* (M^+) calcd 203.095; obsd 203.094.

Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.67; H, 6.43; N, 6.89.

(b) Using oxalylchloride and triethylamine. A solution of oxalyl chloride (Janssen, 0.27 mL, 3.1 mmol) in THF (10 mL) was added at -70°C to a solution of triethylamine (0.43 mL, 3.1 mmol) in THF (30 mL). The reaction mixture (a white slurry) was stirred for 5 min. A solution of 3-benzoylacrylic acid (**5.8**, 528 mg, 3.0 mmol) in THF (10 mL) was added to the mixture at -70°C in 5 min. The mixture was stirred for 30 min allowing the temperature to rise to -30°C. Then a solution of aqueous Me_2NH (40%, 0.50 mL, ca. 3.9 mmol) and triethylamine (0.43 mL, 3.1 mmol) in THF (10 mL) was added at -40°C. The reaction mixture was stirred for 1.5 h, allowing the temperature to rise to 0°C. Work-up by addition of water (20

mL) and Et_2O (20 mL), extraction with ether (3 x 25 mL), drying (brine, $MgSO_4$), filtration and removal of the solvent gave crude **5.6a**, which was purified by bulb-to-bulb distillation at 170°C (0.05 mm Hg). The yield of **5.6a**, isolated as an yellow oil, varied between 34-77%. Crystallization from ethyl acetate/hexane gave analylically pure **5.6a** as an yellow solid, mp 71.0-72.0°C. ^{1}H NMR of the purified product was identical with that of material obtained via procedure (a).

(*E*)-*N,N*-Diethyl-3-(benzoyl)acrylamide (5.6b) was prepared analogously to the procedure (a) described for **5.6a**, using **5.8** (880 mg, 5.0 mmol), DPPCl (0.96 ml, 5.0 mmol), triethylamine (2 x 0.72 mL, 2 x 5.0 mmol) and diethylamine (0.52 mL, 5.0 mmol). The reaction temperature was kept between -10°C to 0°C. Work-up and purification [flash chromatography (silica gel, Et_2O, second fraction)] gave 871 mg (75%) of **5.6b** as a yellow oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.15 (t, J = 7.5 Hz) and 1.18 (t, J = 7.5 Hz, together 3H), 3.19 (q, J = 7.5 Hz) and 3.22 (q, J = 7.5 Hz, together 4H), 7.35-7.58 (m, 4H), 7.93 (d, J = 14.2 Hz) and 7.98 (d, J = 7.5 Hz, together 3H); ^{13}C NMR ($CDCl_3$) δ 12.8 (q), 14.9 (q), 41.0 (t), 42.4 (t), 128.6 (d, 2x), 132.7 (d), 133.4 (d), 133.6 (d), 136.8 (s), 164.0 (s), 189.4 (s); MS *m/z* (M^+) calcd 231.126, obsd 231.126.

(E)-Methyl-*N,N*-diethyl-3-carbamoylacrylate[15] (5.7) was prepared from *N,N*-diethyl-3-carbamoylacrylic acid[15] **5.10** (isolated in a yield of 85% from maleic anhydride and diethylamine[15]). The general procedure described by Ono *et al.* was carried out,[16] using **5.10** (14.5 g, 84 mmol), methyl iodide (Merck, 10 mL, 170 mmol) and DBU (Janssen, 12.8 g, 84 mmol) in benzene (160 mL). Work-up, after reflux for 2 h, by cooling to room temperature, addition of a few drops of 2 N HCl, drying ($MgSO_4$), filtration, removal of the solvent and purification by bulb-to-bulb distillation at 135°C (0.06 mm Hg) gave 13.24 g (85%) of **5.7** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.20 (t, J = 7 Hz) and 1.25 (t, J = 7 Hz, together 6H), 3.30 (q, J = 7 Hz) and 3.40 (q, J = 7 Hz together 4H), 3.75 (s, 3H), 6.00 (d, J = 13 Hz, 1H), 6.65 (d, J = 13 Hz, 1H).

***N,N*-Dimethyl-4-benzoyl-2-(trimethylsilylmethyl)pyrrole-3-carboxamide (5.11).** Triton B (0.80 mL of a 40% w/w solution in methanol, ca. 1.90 mmol) was added dropwise to a solution of isocyanide **5.5** (281 mg, 1.00 mmol) and amide **5.6a** (203

mg, 1.00 mmol) in THF (15 mL) at room temperature. The reaction temperature rose to 24°C during the addition of Triton B. Stirring was continued for 15 min after the addition was complete. Work-up by addition of water (15 mL) and Et_2O (50 mL), separation of the layers, washing of the organic layer with water (2 x 5 mL), drying ($MgSO_4$), filtration and removal of the solvent gave 297 mg (90%) of pyrrole **5.11** as a white solid, mp 132-134°C. Analytically pure material was obtained by crystallization from MeOH, mp 138.0-138.5°C. ^{1}H NMR (DMSO-*d6*) δ 0.01 (s, 9H), 2.05 (br s, 2H), 2.85 (br s, 6H), 3.35 (s, 1H), 7.07 (d, J = 3 Hz, 1H), 7.35-7.90 (m, 5H); ^{13}C NMR (DMSO-*d6*) δ -1,5 (q), 15.6 (t), 34.0 (q), 37.5 (q), 114.0 (s), 121.8 (s), 124.7 (d), 128.1 (d), 128.4 (d), 131.2 (d), 132.5 (s), 139.5 (s), 167.1 (s), 188.7 (s); MS *m/z* (M^+) calcd 328.161, obsd 328.163.

Anal. Calcd for $C_{18}H_{24}N_2O_2Si$: C, 65.82; H, 7.36; N, 8.53. Found: C, 65.42; H, 7.42; N, 8.33.

***N,N*-Dimethyl-4-benzoyl-1-methyl-2-(trimethylsilylmethyl)pyrrole-3-carboxamide (5.12).** Pyrrole **5.11** (460 mg, 1.40 mmol), methyl iodide (0.5 mL, 8.03 mmol) and *n*-Bu_4NI (41 mg, 0.11 mmol) were dissolved in THF (20 mL) and cooled in an icebath for 5 min. After the addition (icebath cooling) of aqueous NaOH (50%, 7 mL) stirring was continued for 30 min at room temperature. Work-up by addition of water (50 mL) and Et_2O (50 mL), separation of the layers, washing of the organic layer with water (2 x 25 mL), drying (brine, $MgSO_4$), filtration and removal of the solvents gave 448 mg (93%) of methylpyrrole **5.12** as a white solid, mp 134-137°C. Analytically pure material was obtained by crystallization from Et_2O/ petroleum ether (bp 60-80°C), mp 138-139°C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.02 (s, 9H), 1.90 (br d, 1H), 2.58 (br d, 1H), 2.79 (s) and 2.84 (s, together 6H), 3.47 (s, 3H), 6.91 (s, 1H), 7.36-7.47 (m, 3H), 7.74 (d, J = 6.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ -1.4 (q), 14.4 (t), 34.2 (q), 38.0 (q), 115.0 (s), 121.3 (s), 127.8 (d), 128.0 (d), 128.5 (d), 131.1 (d), 134.5 (s), 139.4 (s), 167.8 (s), 189.6 (s); MS *m/z* (M^+) calcd 342.176, obsd 342.176.

Anal. Calcd for $C_{19}H_{26}N_2O_2Si$: C, 66.63; H, 7.64; N, 8.18. Found: C, 66.55; H, 7.65; N, 8.16.

4-[1'-(hydroxy)benzyl]-3-(dimethylaminomethyl)-1-methyl-2-(trimethylsilyl-

methyl)pyrrole (5.13). $LiAlH_4$ (Merck, 457 mg, 12 mmol) was added all at once to a solution of pyrrole **5.12** (588 mg, 1.72 mmol) in ether (50 mL) at room temperature and the mixture was stirred for 2 h. Work-up by addition of a few drops of water and aqueous NaOH (15%), stirring for 20 min, drying ($MgSO_4$), filtration and extraction of the solid with Et_2O, removal of the solvents of the combined filtrates gave 520 mg (96%) of **5.13** as a colorless oil, which was pure by ^1H NMR. Analytically pure material was obtained by crystallization from isopropanol, mp 99-100°C. ^1H NMR ($CDCl_3$) δ 0.05 (s, 9H), 2.00 (s, 2H), 2.23 (s, 6H), 2.83 (d, J = 12 Hz, 1H), 3.20 (d, J = 12 Hz, 1H), 5.72 (s, 1H), 6.22 (s, 1H), 7.30-7.88 (m, 5H), 8.05 (br, s, 1H), ^{13}C NMR ($CDCl_3$) δ -1.1 (q), 14.2 (t), 33.6 (q), 43.8 (q), 54.5 (t), 68.9 (d), 113.1 (s), 118.7 (d), 126.1 (d), 126.2 (d), 127.4 (d), 130.0 (s), 144.9 (s); MS *m/z* (M^+) calcd 330.213, obsd 330.214.

Anal. Calcd for $C_{19}H_{30}N_2OSi$: C, 69.04; H, 9.15; N, 8.47. Found: C, 68.88; H, 9.19; N, 8.43.

***N,N*-Dimethyl-4-[1'-(hydroxy)benzyl]-2-(trimethylsilylmethyl)pyrrole-3-carboxamide (5.16).** $LiAlH_4$ (Janssen, 5.0 mL of a 1 M solution in THF, 5 mmol) was added dropwise to a solution of pyrrole **5.11** (315 mg, 0.96 mmol) in THF (20 mL) at room temperature. A solid appeared first during the addition, which disappeared when all $LiAlH_4$ was added to the mixture. After stirring for 5 min, a few drops of water and aqueous NaOH (15%) were added to the reaction mixture. Filtration and extraction of the solid with Et_2O and removal of the solvents of the combined filtrates gave 236 mg (75%) of **5.16** as a colorless oil. ^1H NMR (CD_3OD) δ -0.01 (s, 9H), 1.99 (s, 2H), 2.82 (s, 6H), 5.69 (s, 1H), 6.40 (s, 1H), 7.15-7.45 (m, 5H); ^{13}C NMR ($CDCl_3$) δ -1.7 (q), 17.5 (t), 36.8 (br q), 69.3 (d), 112.6 (s), 114.6 (d), 126.0 (d), 126.1 (d), 127.2 (d), 127.5 (s), 127.9 (s), 130.3 (s), 170.8 (s).

4-Benzoyl-3-phenyl-2-(trimethylsilylmethyl)pyrrole (5.21a). *t*-BuOK (250 mg, 2.23 mmol) was added all at once to a solution of isocyanide **5.5** (281 mg, 1.00 mmol) and chalcone (Fluka, 209 mg, 1.00 mmol) in THF (15 mL) at room temperature. The mixture was stirred for 15 min. Work-up by addition of water (25 mL) and CH_2Cl_2 (50 mL), extraction with CH_2Cl_2 (2 x 20 mL), drying ($MgSO_4$), filtration and removal of the solvents gave 313 mg of crude **5.22a**, which was

purified by crystallization from MeOH/H_2O, mp 180-181°C; yield 263 mg (79%). Analytically pure material was obtained by recrystallization from MeOH, mp 182-183°C. ^{1}H NMR (acetone-*d6*, 300 MHz) δ -0.01 (s, 9H), 2.29 (s, 2H), 7.14 (d, J = 2.9 Hz, 1H), 7.18-7.26 (m, 1H), 7.31-7.42 (m, 4H), 7.44-7.52 (m, 2H), 7.53-7.58 (m, 1H), 7.85 (d, J = 8.3 Hz, 2H); ^{13}C NMR (acetone-*d6*) δ -1.1 (q), 16.0 (t), 121.3 (s), 123.6 (s), 125.8 (d), 126.1 (d), 128.2 (d), 128.6 (d), 129.7 (d), 131.1 (s), 131.3 (d), 131.6 (d), 137.6 (s), 141.8 (s), 190.9 (s); MS *m/z* (M^+) calcd 333.155, obsd 333.156.

Anal. Calcd for $C_{21}H_{23}NOSi$: C, 75.63; H, 6.95; N, 4.20. Found: C, 75.42; H, 7.00; N, 4.18.

Dimethyl 2-(trimethylsilylmethyl)pyrrole-3,4-dicarboxylate (5.22a). *t*-BuOK (250 mg, 2.23 mmol) was added all at once to a solution of isocyanide **5.5** (281 mg, 1.00 mmol) and dimethyl fumarate (216 mg, 1.50 mmol) in THF (15 mL) at room temperature. The reaction mixture was stirred overnight at room temperature. Work-up by addition of water (25 mL) and Et_2O (50 mL), separation of the layers, washing of the organic layer with water (3 x 25 mL), drying (brine, $MgSO_4$), filtration and removal of the solvents gave 210 mg of crude **5.22a**, which was purified by crystallization from EtOH, yielding 200 mg (74%) of pure **5.22a** as a white solid, mp 148-149°C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.11 (s, 9H), 2.50 (s, 2H), 3.90 (s, 6H), 7.23 (d, J = 3 Hz, 1H), 9.20 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ -1.73 (q), 17.8 (t), 51.0 (q), 51.2 (q), 109.4 (s), 115.7 (s), 122.7 (d), 139.4 (s), 164.9 (s), 165.7 (s); MS *m/z* (M^+) calcd 269.109, obsd 269.108.

Anal. Calcd for $C_{12}H_{19}NO_4Si$: C, 53.51; H, 7.11; N, 5.20. Found: C, 53.36; H, 7.16; N, 5.19.

Methyl 4-benzoyl-1-methyl-2-(trimethylsilylmethyl)pyrrole-3-carboxylate (5.23b). Isocyanide **5.5** (843 mg, 3.0 mmol) and methyl 3-benzoylacrylate[26] (600 mg, 3.16 mmol) were dissolved in THF (30 mL) and cooled to 0°C. Triton B (5 mL of a 40% w/w solution in methanol, ca. 4.75 mmol) was added within one min; the temperature rose to 5°C. Stirring was continued for 5 min. Work-up by addition of aqueous NH_4Cl (10%, 20 mL) and Et_2O (100 mL), separation of the layers, washing of the ethereal layer with water (2 x 25 mL), drying (brine, $MgSO_4$),

filtration and removal of the solvents, gave 952 mg of crude *N*-H pyrrole as an orange oil. The orange oil was dissolved in THF (30 mL) and cooled in an ice bath. *t*-BuOK (460 mg, 3.57 mmol) and MeI (1.0 mL, 16.06 mmol) were added sequentially. The mixture was stirred for 15 min at room temperature. Work-up by addition of water (100 mL) and Et_2O (100 mL), separation of the layers, washing of the organic layer with water (2 x 25 mL), drying (brine, $MgSO_4$), filtration and removal of the solvents gave 905 mg of crude **5.23b**, which was purified by filtration over silica gel (Et_2O) to yield 815 mg (82%) pure (by NMR) **5.23b** as a colorless oil, which solidified on standing (-25°C). Crystallization from ethanol gave analytically pure material, mp 87-89°C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.00 (s, 9H), 2.47 (s, 2H), 3.24 (s, 3H), 3.48 (s, 3H), 6.82 (s, 1H), 7.30-7.38 (m, 2H), 7.39-7.47 (m, 1H), 7.73 (d, J = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ -1.1 (q), 15.6 (t), 34.0 (q), 50.1 (q), 110.2 (s), 123.5 (s), 125.5 (d), 127.8 (d), 128.7 (d), 131.6 (d), 139.6 (s), 140.5 (s), 165.2 9s), 191.7 (s); MS *m/z* (M^+) calcd 329.143, obsd 329.145.

Anal. Calcd for $C_{18}H_{23}NO_3Si$: C, 65.62; H, 7.04; N, 4.25. Found: C, 65.37; H, 7.12; N, 4.23.

***N,N*-Diethyl-4-benzoyl-1-methyl-2-(trimethylsilylmethyl)pyrrole-3-carboxamide (5.24b).** Triton B (2.2 mL of a 40% w/w solution in methanol, 5.23 mmol) was added dropwise to a ice-bath cooled solution of isocyanide **5.5** (760 mg, 2.70 mmol) and benzoylacrylamide **5.6b** (675 mg, 2.92 mmol) in THF (30 mL). The mixture was stirred for 30 min at room temperature. Work-up by addition of water (20 mL) and Et_2O (100 mL), separation of the layers, washing of the organic layer with water (2 x 25 mL), drying ($MgSO_4$), filtration and removal of the solvents gave 905 mg of a light yellow solid. This solid was dissolved in THF (20 mL). *t*-BuOK (440 mg, 3.93 mmol) and MeI (1.0 mL, 16.06 mmol) were added to the solution sequentially at 5°C, and the mixture was stirred for 30 min. Work-up by addition of water (50 mL) and Et_2O (100 mL), separation of the layers, washing of the organic layer with water (2 x 30 mL), drying (brine, $MgSO_4$), filtration and removal of the solvents, gave 864 mg of crude **5.24b** as a yellow oil, which was purified by filtration over silica gel (Et_2O) to yield 775 mg (77%) of pure (by NMR) **5.24b** as a slightly yellow oil. Methylpyrrole **5.24b** solidified in Et_2O/hexane

at -25°C, mp 108-109°C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.05 (s, 9H), 0.97 (t, J = 6.8 Hz, 3H), 1.09 (t, J = 7.0 Hz, 3H), 1.93 (br d, J = 15.0 Hz, 1H), 2.34 (br d, J = 15.0 Hz, 1H), 3.13-3.50 (br m) and 2.47 (s, together 7H), 6.87 (s, 1H), 7.34-7.42 (m, 2H), 7.44-7.50 (m, 1H), 7.75 (d, J = 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ -0.1 (q), 12.4 (q), 13.5 (q), 14.5 (t), 34.3 (q), 38.3 (t), 42.7 (t), 116.0 (s), 121.1 (s), 127.8 (d), 127.9 (d), 128.6 (d), 131.0 (d), 133.6 (s), 139.6 (s), 167.2 (s), 189.2 (s); MS *m/z* (M^+) calcd 370.206, obsd 370.206.

Anal. Calcd for $C_{22}H_{31}N_2O_2Si$: C, 68.01; H, 8.16; N, 7.56. Found: C, 67.86; H, 8.22; N, 7.53.

4-Benzoyl-3-[(*E*)-2'-phenylethenyl]-1-methyl-2-(trimethylsilylmethyl)pyrrole (5.25b). *t*-BuOK (750 mg, 6.70 mmol) was added all at once to a solution of isocyanide **5.5** (843 mg, 3.00 mmol) and (*E*),(*E*)-1,5-diphenylpenta-1,3-dien-5-one[27] (702 mg, 3.00 mmol) in THF (80 mL) at room temperature. The mixture was stirred for 10 min. Potassium tosylate was removed by extracting with water (2 x 10 mL). If necessary, some brine was added to achieve a better separation of the layers. MeI (1.5 mL, 24.0 mmol), *n*-Bu_4NI (87 mg, 0.23 mmol) and aqueous NaOH (50%, 15 mL) were added to the THF layer sequentially at room temperature. The reaction mixture was stirred for 30 min. Work-up by addition of water (100 mL) and Et_2O (100 mL), separation of the layers, washing of the organic layer with water (2 x 50 mL), drying (brine, $MgSO_4$), filtration and removal of the solvents, gave 1.07 g of crude **5.25b**, which was purified by filtration over Al_2O_3 (neutral, Et_2O) to yield 947 mg (84%) of pure **5.25b** as a dark yellow solid, mp 131.5-132.5°C. Analytically pure material was obtained by crystallization form petroleum ether (bp 60-80°C), mp 135.5-136.5°C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.05 (s, 9H), 2.23 (s, 2H), 3.42 (s, 3H), 6.78 (s, 1H), 6.93 (d, J = 17.0 Hz, 1H), 7.10 (dd, J = 7 Hz and 7 Hz, 2H), 7.23 (dd, J = 8 and 7 Hz, 2H), 7.30-7.47 (m, 5H), 7.74 (d, J = 7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ -0.7 (q), 15.2 (t), 34.5 (q), 117.7 (s), 120.9 (s), 122.5 (d), 125.7 (d), 126.1 (d), 127.3 (d), 127.8 (d), 128.2 (d), 128.9 (d), 130.6 (d), 130.9 (d), 133.2 (s), 138.8 (s), 140.8 (s), 191.3 (s); MS *m/z* (M^+) calcd 373.186, obsd 373.186.

Anal. Calcd for $C_{24}H_{27}NOSi$: C, 77.16; H, 7.28; N, 3.75. Found: C, 77.19; H,

7.36; N, 3.68.

2-Isocyano-2-tosyl-1-(trimethylsilyl)propane (5.26). *t*-BuOK (1.40 g, 12.5 mmol) was added all at once to a solution of isocyanide **5.5** (2.81 g, 10 mmol) in THF (60 mL) at -5°C. After stirring for 5 min, MeI (5.0 mL, 161 mmol) was added all at once to the reaction mixture, which was stirred for an additional hour at room temperature. Work-up by addition of water (50 mL) and Et_2O (100 mL), separation of the layers, washing of the organic layers with water (2 x 50 mL), drying (brine, $MgSO_4$), filtration and removal of the solvents gave crude **5.26** (2.8 g), which was purified by filtration over silica gel (Et_2O), yielding 2.73 g (92%) of pure **5.26** as a white solid, mp 86-88°C. Analytically pure material was obtained by crystallization from MeOH, mp 88.5-90.0°C. ^{1}H NMR (CCl_4) δ 0.15 (s, 9H), 1.20-1.45 (m, 2H), 1.58 (s, 3H), 2.43 (s, 3H), 7.35 (d, J = 8.5 Hz, 2H), 7.85 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 0.0 (q), 21.6 (t), 21.9 (q), 23.1 (q), 78.0 (s), 128.7 (s), 129.6 (d), 131.4 (d), 146.0 (s), 163.7 (s). IR (KBr) 3060, 2950, 2125, 1595, 1405, 1320, 1300, 1255, 1220, 1150, 1100, 1070, 1040, 1025, 850,720, 700 cm^{-1}.

Anal. Calcd for $C_{14}H_{21}NO_2SSi$: C, 56.91; H, 7.16; N, 4.74; S, 10.85. Found: C, 56.94; H, 7.12; N, 4.58; S, 10.65.

2-Isocyano-2-tosyl-1-(trimethylsilyl)butane (5.27) was prepared analogously to the procedure of **5.26** using isocyanide **5.5** (562 mg, 2.00 mmol), *t*-BuOK (300 mg, 2.68 mmol) and EtI (1.0 mL, 13.0 mmol) in THF (20 mL). After stirring for 3 h and work-up, 550 mg of crude **5.27** was isolated and purified by filtration over silica gel (Et_2O) to yield 500 mg (81%) of **5.27** as a colorless oil, which was crystallized from *i*PrOH, mp 80-82°C. ^{1}H NMR (CCl_4) δ 0.19 (s, 9H), 1.04 (t, J = 7 Hz, 3H), 1.35 (s, 2H), 1.92 (q, J = 7 Hz, 2H), 2.49 (s, 3H), 7.35 (d, J = 8 Hz, 2H), 7.81 (d, J = 8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ -0.2 (q), 8.7 (q), 21.0 (t), 21.6 (q), 29.6 (t), 81.8 (s), 129.5 (d), 129.8 (s), 131.1 (d), 145.8 (s), 163.7 (s); IR (KBr) 3050, 2950, 2140, 1450, 1415, 1300, 1255, 1220, 1145, 1110, 1080, 950, 840, 770, 680 cm^{-1}; MS *m/z* (M^+) calcd 309.122, obsd 309.122.

Anal. Calcd for $C_{15}H_{23}NO_2SSI$: C, 58.21; H, 7.49; N, 4.53; S, 10.36. Found: C, 57.96; H, 7.60; N, 4.50; S, 10.46.

2-Isocyano-1-phenyl-2-tosyl-3-(trimethylsilyl)propane (5.28). *t*-BuOK (230 mg,

2.05 mmol) was added all at once to a solution of isocyanide **5.5** (562 mg, 2.00 mmol) in THF (15 mL) at -40°C. After stirring for 5 min at the same temperature, benzyl bromide (Merck, 0.24 mL, 2.02 mmol) was added all at once to the reaction mixture, which was stirred for another 2 h under ice-bath cooling. Work-up by addition of water (25 mL) and Et_2O (50 mL), extraction with Et_2O (1 x 25 mL), drying (brine, $MgSO_4$), filtration and removal of the solvents gave a residue (760 mg) containing **5.28** and some benzyl bromide. Purification by crystallization from *i*PrOH gave 522 mg (70%) of analytically pure **5.28**, mp 125-126°C. ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9H), 1.29 (d, J = 13.5 Hz, 1H), 1.66 (d, J = 13.5 Hz, 1H), 2.52 (s, 3H), 3.21 (s, 2H), 7.38 (s) and (7.45 (d, J = 8 Hz, together 7H), 8.00 (d, J = 8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ -0.7 (q), 21.0 (t), 21.7 (q), 42.5 (t), 81.3 (s), 127.9 (d), 128.4 (d), 129.0 (s), 129.6 (d), 130.9 (d), 131.4 (d), 132.2 (s), 146.1 (s), 164.9 (s); IR (KBr) 3060, 2920, 2138, 1550, 1450, 1400, 1320, 1250, 1140, 1090, 1035, 845, 820, 760, 730, 705, 690, 670 cm^{-1}; MS m/z (M^+) calcd 371.138, obsd 371.136.

Anal. Calcd for $C_{20}H_{25}NO_2SSi$: C, 64.65; H, 6.78; N, 3.77; S, 8.63. Found: C, 64.68; H, 6.85; N, 3.59; S, 8.53.

4-Isocyano-4-tosyl-5-trimethylsilyl-1-pentene (5.29) was prepared analogously to the procedure described for **5.26**, using isocyanide **5.5** (562 mg, 2.00 mmol), *t*-BuOK (300 mg, 2.68 mmol) and allyl bromide (Janssen, 1.8 mL, 20.7 mmol) in THF (20 mL). The reaction mixture was stirred for 2 h at 0°C. Crude **5.29** (576 mg), isolated after usual work-up, was purified by crystallization from *i*PrOH at -25°C. Isocyanide **5.29** was not obtained as a solid: at room temperature the solid melted to an unstable oil; yield: 521 mg (79%). ^{1}H NMR ($CDCl_3$) δ 0.10 (s, 9H), 1.35 (s, 2H), 2.45 (s) and 2.50 (d, J = 14 Hz, together 5H), 4.85-5.35 (m, 2H), 5.40-5.90 (m, 1H), 7.35 (d, J = 8 Hz, 2h), 7.91 (d, J = 8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ -0.2 (q), 21.0 (t), 21.5 (q), 40.7 (t), 80.7 (s), 120.9 (t), 129.5 (d), 129.5 (d), 131.2 (d), 146.0 (s), 164.3 (s).

Methyl 2-[3'-benzoyl-2'-(phenyl)propyl]-4-benzoyl-1-methylpyrrole-3-carboxylate (5.30) and **methyl 4-benzoyl-1,2-dimethylpyrrole-3-carboxylate (5.33).** A solution of pyrrole **5.23b** (565 mg, 1.71 mmol) in THF (10 mL) was added in 5 min to a suspension of TASF (550 mg, 2.00 mmol) and chalcone (Fluka, 356 mg, 1.71

mmol) in THF (20 mL) at -50°C. The cooling bath was removed and the reaction mixture was stirred for 1 h. Work-up by addition of saturated NH_4Cl (10 mL), extraction with Et_2O (2 x 20 mL), drying (brine, $MgSO_4$), filtration and removal of the solvents gave a residu (850 mg) which contained **5.30**, **5.33** and chalcone. This mixture was separated using flash chromatography (silica gel, Et_2O). The first fraction consisted of chalcone (158 mg), the second fraction contained 320 mg (40%) of **5.30** (pure by NMR) and the third fraction contained 111 mg (25%) of **5.33** (pure by NMR). Compounds **5.30** and **5.33** were obtained analytically pure by crystallization from EtOH. Data of **5.30**: mp 172.5-173.5°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.86-2.95 (m, 1H), 3.00 (s, 3H), 3.16 (dd, J = 16.5 and 4.1 Hz, 1H), 3.25-3.31 (m, 1H), 3.35 (s, 3H), 3.53-3.68 m, 2H), 6.70 (s, 1H), 6.98-7.18 (m, 7H), 7.20-7.29 (m, 3H), 7.30-7.43 and 7.39 (d, J = 7.5 Hz, together 3H), 7.71 (d, J = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 31.7 (t), 33.9 (d), 40.1 (q), 43.3 (t), 50.2 (q), 113.6 (s), 123.2 (s), 126.6 (d), 127.4 (d), 127.5 (d), 127.7 (d), 128.0 (d), 128.1 (d), 128.3 (d), 128.5 (d), 131.5 (d), 132.8 (d), 136.6 (s), 137.5 (s), 138.4 (s), 143.6 (s), 165.0 (s), 191.2 (s), 197.9 (s); MS *m/z* (M^+) calcd 465.194, obsd 465.194.

Anal. Calcd for $C_{30}H_{27}NO_4$: C, 77.40; H, 5.85; N, 3.01. Found: C, 77.49; H, 5.92; N, 3.00.

Data of **5.33**: mp 137-138°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2,40 (s, 3H), 3.30 (s, 3H), 3.50 (s, 3H), 6.84 (s, 1H), 7.30-7.39 (m, 2H), 7.40-7.45 (m, 2H), 7.73 (dd, J = 8.4 and 1.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 10.4 (q), 33.8 (q), 50.4 (q), 112.5 (s), 123.2 (s), 126.0 (d), 127.8 (d), 128.6 (d), 131.6 (d), 136.3 (s), 139.3 (s), 165.1 (s), 191.2 (s); MS *m/z* (M^+) calcd 257.105, obsd 257.103.

Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: 69.65; H, 5.88; N, 5.33.

4-Benzoyl-2-[2'-hydroxy-4'-phenyl-but-3'-enyl]-3-[(*E*)-2'-phenylethenyl]-1-methyl-pyrrole (5.31). A solution of pyrrole **5.25b** (374 mg, 1.00 mmol) in THF (10 mL) was added in 5 min to a suspension of TASF (480 mg, 1.75 mmol) and cinnamaldehyde (198 mg, 1.50 mmol) in THF (15 mL) at room temperature. Stirring was continued overnight. Work-up by addition of $NaHSO_3$ solution (20%, 15 mL), stirring for 1.5 h, separation of the layers, washing of the organic layer with

$NaHSO_3$ (20%, 1 x 15 mL) and saturated NH_4Cl (10 mL), drying ($MgSO_4$), filtration and removal of the solvents gave a residu (515 mg), which was purified by flash chromatography (silica gel). The first fraction (CH_2Cl_2) contained mainly methylpyrrole **5.34** (68 mg). The second fraction (CH_2Cl_2/ethyl acetate 1:1) contained 320 mg (74%, pure by ^1H NMR) of **5.31** as a white solid, mp 160-162°C. Analytically pure material was obtained by crystallization from benzene/hexane, mp 165-167°C. ^1H NMR (DMSO-*d6*, 300 MHz) δ 3.98-4.04 (d, J = 6.8 Hz, 2H), 3.64 (s, 3H), 4.45 (br s, 1H), 5.36 (d, J = 5.4 Hz, 1H), 6.39 (dd, J = 16.3 and 6.0 Hz, 1H), 6.55 (d, J = 16.3 Hz, 1H), 6.93 (d, J = 16.2 Hz, 1H), 7.10-7.54 (m) and 7.19 (s, together 15 H), 7.65 (d, J = 7.5 Hz, 2H); ^{13}C NMR (DMSO-*d6*) δ 33.1 (t), 34.7 (q), 71.3 (d), 119.8 (s), 120.0 (s), 122.7 (d), 125.6 (d), 126.2 (d), 126.6 (d), 127.4 (d), 128.1 (d), 128.2 (d) (2x), 128.6 (d) (3x), 131.1 (d), 131.7 (s), 132.1 (d), 133.4 (d), 136.7 (s), 138.5 (s), 140.6 (s), 190.3 (s); MS *m/z* (M^+) calcd 433.204, obsd 433.203.

Anal. Calcd for $C_{30}H_{27}NO_2.½H_2O$: C, 81.42; H, 6.38; N, 3.16. Found: C, 81.06; H, 6.15; N, 2.82.

4-Benzoyl-2-[2'-hydroxy-2'-(*p*-nitro)phenylethyl]-3-[2'-phenylethenyl]-1-methylpyrrole (5.32). A solution of pyrrole **5.25b** (374 mg, 1.00 mmol) and *p*-nitro benzaldehyde (Merck, 151 mg, 1.00 mmol) in THF (10 mL) was added in 5 min to a suspension of TASF (500 mg, 1.82 mmol) in THF (10 mL) at -70°C. The cooling bath was removed and the reaction mixture was stirred for 1 h. The temperature rose to -10°C during that period. Work-up by addition of saturated NH_4Cl (20 mL) and Et_2O (25 mL), extraction with Et_2O (1 x 25 mL), drying (brine, $MgSO_4$), filtration and removal of the solvents gave 462 mg of crude **5.32**, mp 195-199°C, which was purified by crystallization[28] from toluene to yield 318 mg (66%) of analytically pure **5.32**, mp 209-211°C. ^1H NMR (DMSO-*d6*, 300 MHz) δ 3.16-3.31 (m, 2H), 3.60 (s, 3H), 5,08 (br s, 1H), 6.02 (s, 1H), 6.91 (d, J = 16.2 Hz, 1H), 7.22-7.42 (m, 7H), 7.48-7.70 (m) and 7.53 (d, J = 7.5 Hz) and 7.62 (d, J = 7.8 Hz) and 7.56 (d, J = 7.5 Hz, together 5H), 7.75 (d, J = 7.5 Hz, 2H), 8.20 (d, J = 8.1 Hz, 2H); ^{13}C NMR (DMSO-*d6*) δ 34.5 (q), 34.6 (t), 71.5 (d), 119.7 (s), 120.4 (s), 122.2 (d), 123.2 (d), 125.6 (d), 126.6 (d), 126.9 (d), 127.4 (d), 128.2 (d), 128.5 (d),

128.7 (d), 130.6 (s), 131.2 (d), 132.0 (d), 138.3 (s), 140.6 (s), 146.5 (s), 152.9 (s), 190.3 (s); MS *m/z* (M^+) calcd 452.174, obsd 452.174.

Anal. Calcd for $C_{28}H_{24}N_2O_4.½H_2O$: C, 72.89; H, 5.46; N, 6.07. Found: C, 73.15; H, 5.35; N, 6.05.

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